



- 14 -

RECEIVED

JAN 22 2002

TECH CENTER 1600/2900

REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested. Pursuant to 37 CFR § 1.121, attached as Appendix A is a Version With Markings to Show Changes Made.

The rejection of claims 3-47 under 35 U.S.C. § 112, second paragraph, for indefiniteness is respectfully traversed in view of the above amendments and the following remarks.

It is the position of the U.S. Patent and Trademark Office ("PTO") that claim 10 is broader than claim 7 and claim 11 is broader than claim 10. Applicants respectfully disagree. In particular, claim 10 requires all of the limitations of claim 7 and further defines the oxidizing step as including "cooling the reaction mixture; and adding water to the reaction mixture, whereby a sediment containing betulonic aldehyde forms." Thus, claim 10 is narrower than claim 7. In addition, claim 11 requires all of the limitations of claim 10 and further defines the method of claim 10 as including the additional step of "recrystallizing the sediment" formed in claim 10. Thus, claim 11 is narrower than claim 10.

In view of the all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

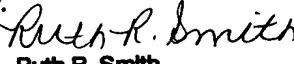
Date: November 8, 2001


Georgia Evans
Registration No. 44,597

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603
Telephone: (716) 263-1672
Facsimile: (716) 263-1600

Certificate of Mailing - 37 CFR 1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date below.

Nov. 8, 2001 | 
Date | Ruth R. Smith



- 1 -

Appendix A

Version With Markings to Show Changes Made

RECEIVED

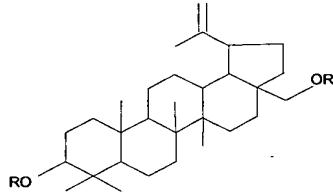
JAN 22 2002

TECH CENTER 1600/2900

In reference to the amendments made herein to claims 3, 7, 10, 11, 14, 16, 17, 19, 21-23, 26, 28-36, 38, 39, 41, 45, and 46, additions appear as underlined text, while deletions appear as bracketed text, as indicated below:

In the Claims:

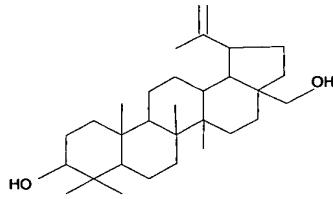
3. (Amended) A method of synthesizing a diether having the formula:



wherein R is alkyl,

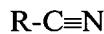
said method comprising:

[providing] alkylating a dialcohol having the formula:



[and

alkylating the dialcohol] with a nitrile having the formula:



under conditions effective to form the diether, and
isolating the diether.

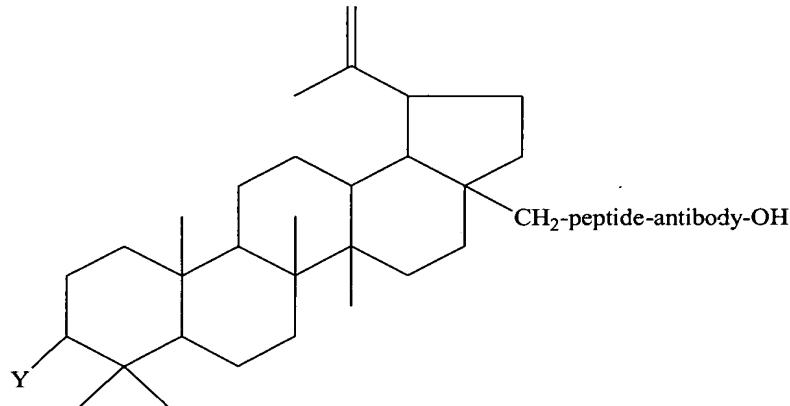
7. (Amended) A method of preparing betulonic aldehyde comprising: oxidizing betulinol with chromium anhydride in acetone in the presence of sulfuric acid under conditions effective to produce betulonic aldehyde, and isolating the betulonic aldehyde.

10. (Amended) A method according to claim 7 [further comprising, after said oxidizing:] , wherein said oxidizing further comprises:
cooling the reaction mixture; and
adding water to the reaction mixture, whereby a sediment containing betulonic aldehyde forms.

14. (Twice-Amended) A compound according to claim 13, wherein the pentapeptide is -Gly-Ala-Leu-Gly-Leu- ([SEQ. ID. No.] SEQ ID NO: 2).

16. (Twice-Amended) A compound according to claim 15, wherein the tetrapeptide is -Leu-Ala-Leu-Ala- ([SEQ. ID. No.] SEQ ID NO: 1).

17. (Amended) A method of producing a betulinol-antibody conjugate having the formula:

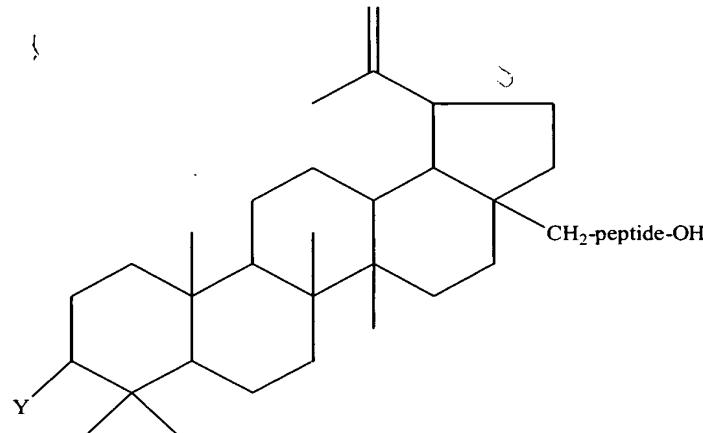


wherein

Y is a hydroxy group, an aikoxyl group, or an alkanoyloxy group,

said method comprising:

[providing] reacting a betulinol peptide having the formula:



[and

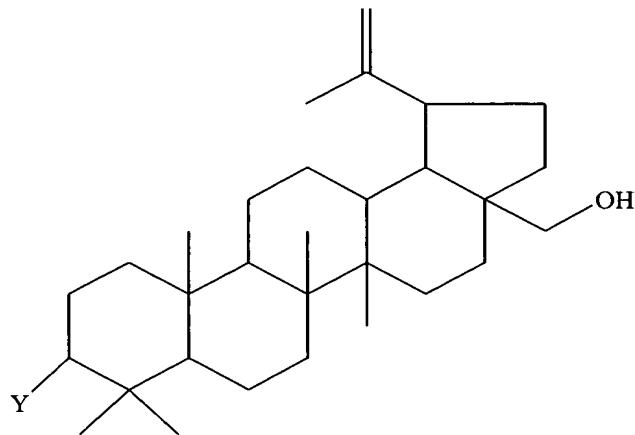
converting the betulinol peptide] with an antibody having the formula H-antibody-OH under conditions effective to produce the betulinol-antibody conjugate, and isolating the betulinol-antibody conjugate.

19. (Twice-Amended) A method according to claim 18, wherein the pentapeptide is -Gly-Ala-Leu-Gly-Leu- ([SEQ. ID. No.] SEQ ID NO: 2).

21. (Twice-Amended) A method according to claim 20, wherein the tetrapeptide is -Leu-Ala-Leu-Ala- ([SEQ. ID. No.] SEQ ID NO: 1).

22. (Amended) A method according to claim 17, wherein said [providing the] betulinol peptide is obtained by a process comprising [comprises]:

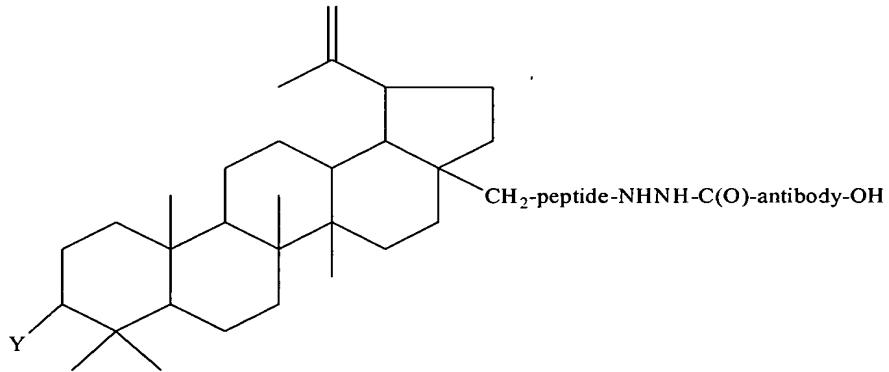
[providing] reacting a compound having the formula:



[and

converting the compound] with a peptide having the formula H-peptide-OH under conditions effective to produce the betulinol peptide, and isolating the betulinol peptide.

23. (Amended) A method of producing a betulinol-antibody conjugate having the formula:

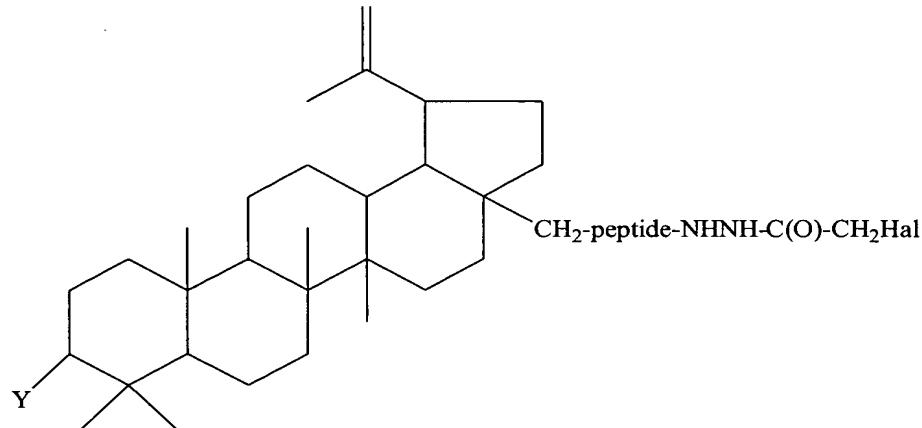


wherein

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

said method comprising:

[providing] reacting a haloacetylhydrazide having the formula:



wherein

Hal is a halogen

[and

converting the haloacetylhydrazide] with an antibody having the formula H-antibody-OH under conditions effective to produce the betulinol-antibody conjugate, and

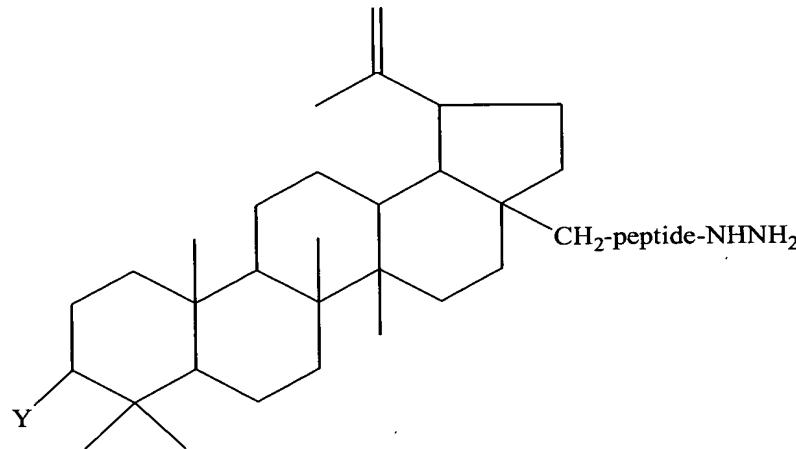
isolating the betulinol-antibody conjugate.

26. (Twice-Amended) A method according to claim 25, wherein the pentapeptide is -Gly-Ala-Leu-Gly-Leu- ([SEQ. ID. No.] SEQ ID NO: 2).

28. (Twice-Amended) A method according to claim 27, wherein the tetrapeptide is -Leu-Ala-Leu-Ala- ([SEQ. ID. No.] SEQ ID NO: 1).

29. (Amended) A method according to claim 23, wherein said [providing a] haloacetylhydrazide is obtained by a process comprising [comprises]:

[providing] reacting a hydrazide having the formula:

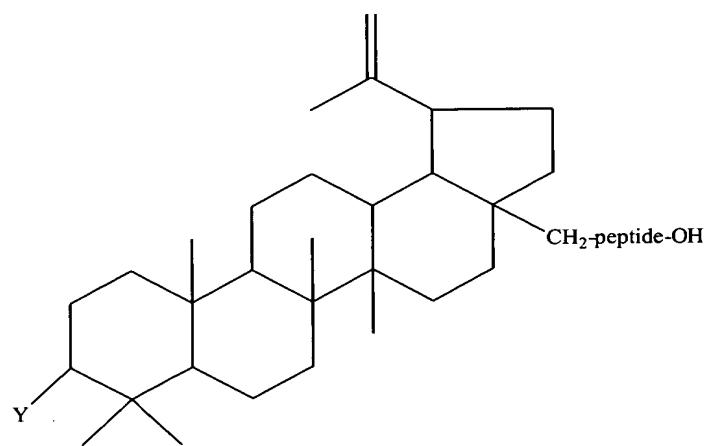


[and

converting the hydrazide] with a [p-nitrophenyl haloacetate] para-nitrophenyl α -haloacetate under conditions effective to produce the haloacetylhydrazide, and isolating the haloacetylhydrazide.

30. (Amended) A method according to claim 29, wherein said [providing a] hydrazide is obtained by a process comprising [comprises]:

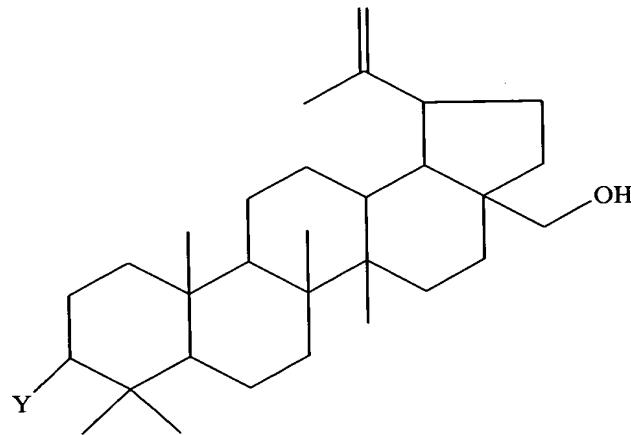
[providing] reacting a betulinol peptide having the formula:



[and

converting the betulinol peptide] with hydrazine hydrate under conditions effective to produce the hydrazide, and isolating the hydrazide.

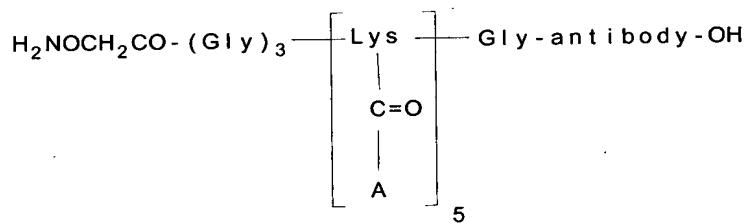
31. (Amended) A method according to claim 30, wherein said [providing the] betulinol peptide is obtained by a process comprising [comprises]: [providing] reacting a compound having the formula:



[and

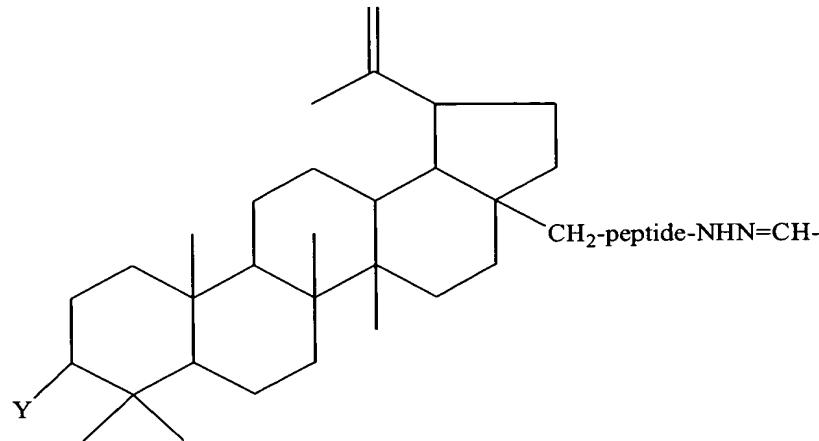
converting the compound] with a peptide having the formula H-peptide-OH under conditions effective to produce the betulinol peptide, and isolating the betulinol peptide.

32. (Amended) A betulinol-antibody conjugate having the formula:



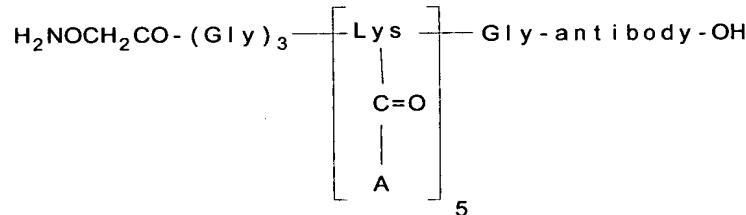
wherein

each [A are] "A" moiety is independently selected from the group consisting of a -CHO group [or] and a moiety having the formula:



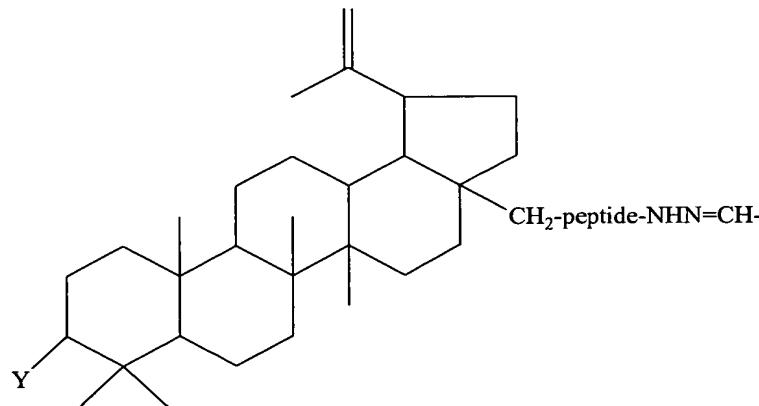
provided that at least one of A is not -CHO; and
Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group.

33. (Amended) A method of producing a betulinol-antibody conjugate having the formula:



wherein

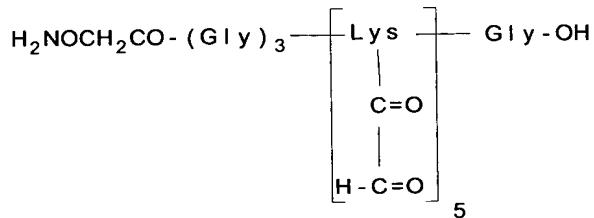
each [A are] "A" moiety is independently selected from the group consisting of a -CHO group [or] and a moiety having the formula:



provided that at least one of A is not -CHO; and
Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

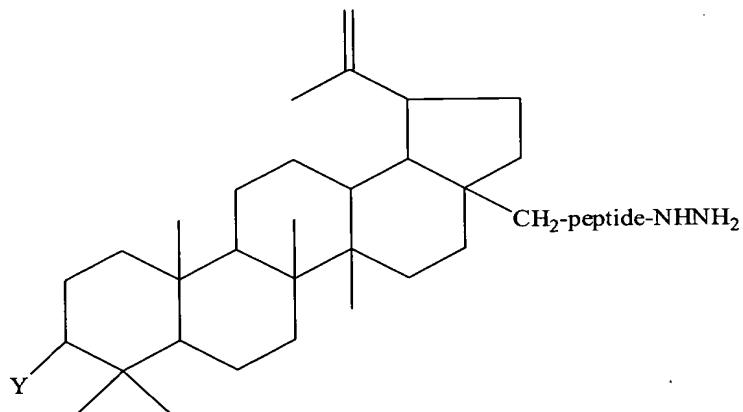
said method comprising:

[providing] reacting a carrier molecule having the formula:



[and

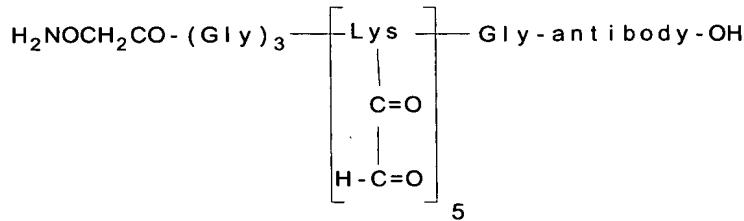
converting the carrier molecule] with a hydrazide having the formula:



and an antibody having the formula H-antibody-OH under conditions effective to produce the betulinol-antibody conjugate, and

isolating the betulinol-antibody conjugate.

34. (Amended) A method according to claim 33, wherein said [converting] reacting the carrier molecule comprises:
reacting the carrier molecule with the antibody under conditions effective to produce an antibody-bound carrier molecule having the formula:

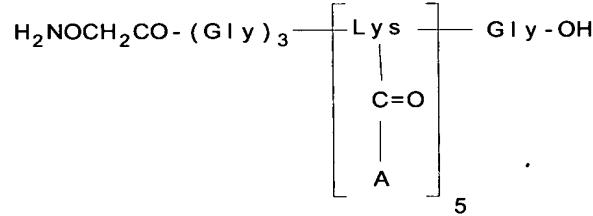


and

[converting] reacting the antibody-bound carrier molecule with the hydrazide under conditions effective to produce the betulinol-antibody conjugate.

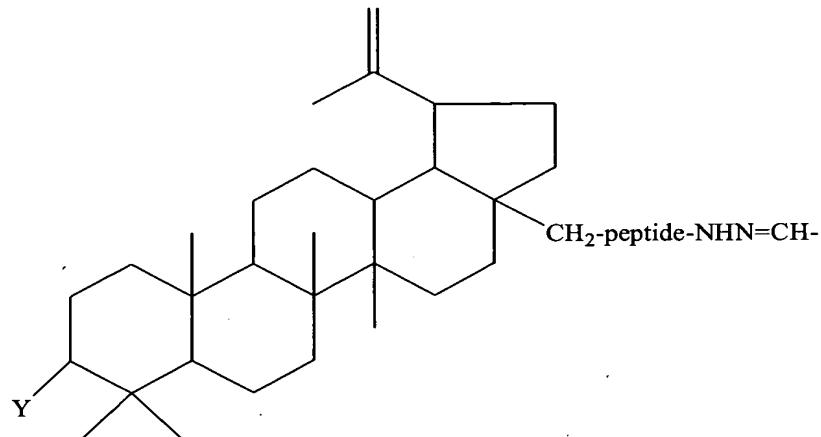
35. (Amended) A method according to claim 33, wherein said [converting] reacting the carrier molecule comprises:

reacting the carrier molecule with the hydrazide under conditions effective to produce a betulinol-bound carrier molecule having the formula:



wherein

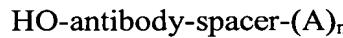
at least one A is a moiety having the formula:



and

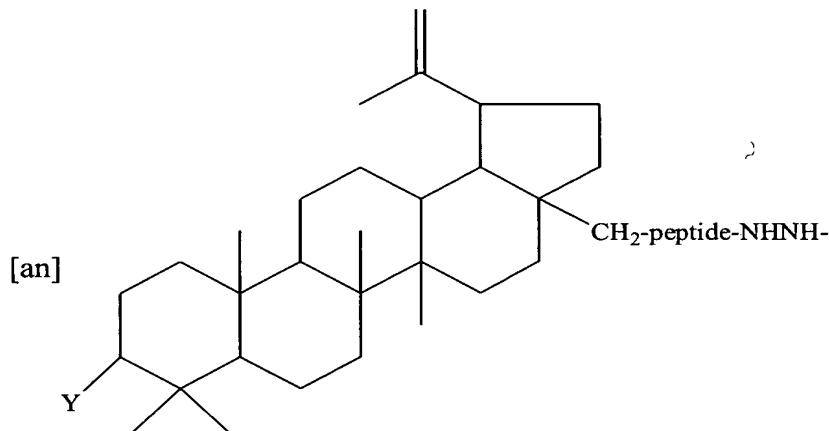
[converting] reacting the betulinol-bound carrier molecule with the antibody under conditions effective to produce the betulinol-antibody conjugate.

36. (Amended) A betulinol-antibody conjugate having the formula:



wherein

A is a moiety having the formula:



Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group; and

n is an integer from 1 to 100.

38. (Amended) A betulinol-antibody conjugate according to claim 36, wherein [spacer] "spacer" is a diamine derivative of polyethylene glycol having 2-(pyridyldithio)-propionyl and N-hydroxysuccinimide ester groups bonded thereto.

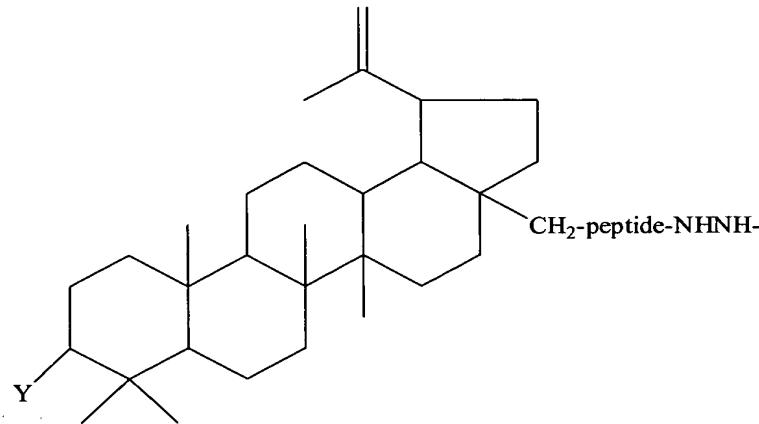
39. (Amended) A betulinol-antibody conjugate according to claim 36, wherein [spacer] "spacer" is a branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester.

41. (Amended) A method of producing a betulinol-antibody conjugate having the formula:

HO-antibody-spacer-(A)_n

wherein

A is a moiety having the formula:



Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group; and

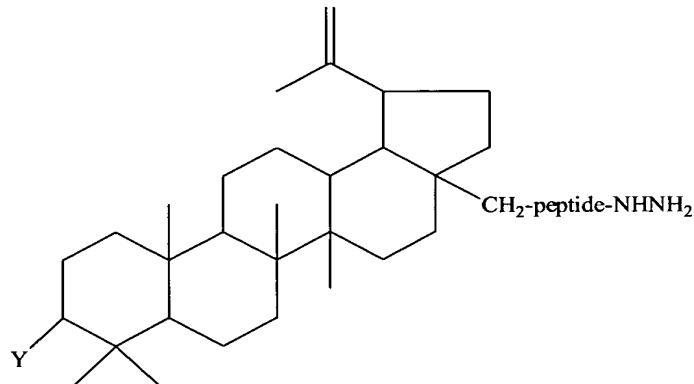
n is an integer from 1 to 100,

said method comprising:

providing a [crosslinker] “spacer” having a first reactive terminus and one or more second reactive termini;

reacting an antibody with the first reactive terminus; [and]

reacting a hydrazide having the formula:



with one or more of the one or more second reactive termini under conditions effective to produce the betulinol-antibody conjugate; and

isolating the betulinol-antibody conjugate.

45. (Amended) A method according to claim 41, wherein [spacer] "spacer" is a diamine derivative of polyethylene glycol having 2-(pyridyldithio)-propionyl and N-hydroxysuccinimide ester groups bonded thereto.

46. (Amended) A method according to claim 41, wherein [spacer] "spacer" is a branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester.